

ABSTRACT OF THE DISCLOSURE

The present disclosure provides an effective method for the refolding of denatured proteins in solution so that properly folded, biologically active protein in solution is recovered in high yield. The refolding takes place at pressures between about 0.25 kbar to about 3.5 kbar, advantageously at about 1.5 kbar to about 3 kbar. Typically a chaotropic agent is present at a concentration which is not effective for denaturing protein at atmospheric pressure, and optionally, oxidation-reduction reagents can be incorporated in the refolding solution so that native intramolecular disulfide bonds can be formed where that is desired. The method is applicable to substantially all proteins, especially after solubilization and/or denaturation of insoluble protein aggregates, inclusion bodies, or abnormal oligomeric (soluble) aggregates.